REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claims 42, 45-49, 51, 52, 54, 55, 58, 61 and 64-66 stand rejected under 35 USC 103 as allegedly being obvious over Meers et al (USP 6,087,325) in view of Parente et al. The rejection is again traversed.

As pointed out previously, claim 42 relates to a highly sensitive method for detecting target cells in a sample. The method comprises treating the sample with lipid vesicle particles, targeted to a targeted cell type. The particles have at least one layer of enveloping lipids and incorporate a cytolytic peptide that is non-covalently attached thereto. In response to a metabolic signal from the target cells, the cytolytic peptide interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer. Permeability of the particles is thereby modulated. The particles also incorporate a species that is activated upon such modulation of permeability and the species is directly or indirectly monitored. Independent claim 64 requires that the metabolic signal comprise a change in pH.

Since the methods disclosed in Meers et al and Parente et al are intrinsically incompatible, one skilled in the art would not have considered combining their teachings and nothing in the citations themselves could have motivated their combination.

Meers et al discloses the use of a non-cytolytic stabilizing peptide that is covalently attached to the hydrophilic lipid head groups of the lipid layer of the liposome for treating diseases. The peptide acts as a blocking group to stabilize intrinsically unstable liposomes. Upon peptidase cleavage of the peptide, the bilayer structure of the membrane destabilizes,

thereby causing the unstable liposome to fall apart by virtue of disruption of the aqueous periphery as opposed to the hydrocarbon phase.

The lipid vesicle particles of the present invention are clearly different from the liposomes disclosed of Meers et al. The lipid vesicle particles of the invention have at least one layer of enveloping lipids and incorporate a cytolytic peptide, which is non covalently attached. The Examiner acknowledges that Meers et al does not teach the use of liposomes that incorporate cytolytic peptides. However, the Examiner contends that it would have been obvious to combine Meers et al with Parente et al's disclosure of the peptide, GALA (i.e. a cytolytic peptide). Applicants again disagree.

Meers et al relates to a method of treating diseases while Parente et al reports the results of a study designed to investigate the effect of GALA on pre-formed liposomes with regard to leakage of vesicle contents. As pointed out previously, the study involved production of vesicles having a "detectable content" and incubating these vesicles in the presence of GALA (right hand column on page 8721 at lines 13 and also at line 44). The effect of the GALA on inducing leakage of the vesicle contents was then investigated. Parente et al discloses the mechanism of leakage (page 827), which involves incorporation of the GALA in the lipid bilayer to produce a channel.

Thus, Parente et al is a study of the mechanism by which GALA, added separately to liposomes, induces leakage of liposome content. In contrast, and in accordance with the present invention, lipid vesicle particles having at least one layer of enveloping lipids and incorporating a cytolytic peptide are used to treat a sample. In response to a metabolic signal from the targeted cell, the cytolytic peptide interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles.

Applicants submit that no basis exists for combining the liposomes of Meers et al, which destabilize upon cleavage of the non-cytolytic peptide blocking group covalently attached to the hydrophilic lipid head group of the lipid layer of the liposome, with the cytolytic peptide of Parente et al. Nothing in Meers et al would have suggested the use of a means of effecting permeabilization of the liposome, other than the one specifically taught by Meers et al. It is only by taking into account knowledge gleaned from Applicants' disclosure that the Examiner could contend otherwise. As the Examiner acknowledges, this type of reconstruction is improper. Further, even if one had looked to Parente et al, one would not have found a suggestion of the present detection method which, unlike Parente et al, involves the use of lipid vesicle particles "having at least one layer of enveloping lipid and incorporating a cytolytic peptide". In summary, nothing but hindsight would have resulted in the combination upon which the Examiner relies and, even if such a combination had been made, one would not have arrived at the present invention.

In view of the above, reconsideration is again requested.

Claim 50 stands rejected under 35 USC 103 as allegedly being obvious over Meers et al in view of Parente et al and further in view of Li et al. The rejection is again traversed.

The fundamental failings of Meers et al, taken alone or in combination with Parente et al, are detailed above. Nothing in any teachings of Li et al regarding the use of binding agents would have cured those deficiencies. Accordingly, reconsideration is again requested.

Claims 56-57 stand rejected under 35 USC 103 as allegedly being obvious over Meers et al in view of Parente et al and further in view of Levinson et al. The rejection is again traversed.

The distinctions between the present invention and the combination of Meers et al and Parente et al are discussed above. The addition of Levinson et al's teachings relating to delivery

would not have brought one skilled in the art any close to the present invention. Accordingly, reconsideration is again requested.

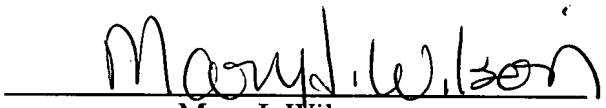
Claim 59 stands rejected as obvious over Meers et al in view of Parente et al and Robinson et al. Claim 60 stands rejected as obvious over Meers et al in view of Parente et al and Blondin et al. These rejections are also again traversed.

Any teaching in Robinson et al relating to the analysis of food stuffs and any teaching in Blondin et al relating to detection of toxins in water samples would not have cured the failings of Meers et al and Parente et al (discussed in detail above) and thus would not have rendered obvious the subject matter of claims 59 and 60, respectively. Reconsideration is again requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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